Serial No.: 10/789,081 Filed: February 27, 20

Filed: February 27, 2004 Page: Page 2 of 21

Amendments to the Claims:

The following listing replaces all previous listings of the claims:

1. (Currently amended) A probe array for qualitative and/or quantitative detection of target molecules in a sample by molecular interactions between probe molecules and target molecules on the probe array, comprising

an array surface, and

a first cleavage product of a first probe molecule, wherein the first cleavage product of the first probe molecule is bound to a first region of a target molecule, and wherein the first cleavage product of the first probe molecule includes a label;

a second cleavage product of the first probe molecule molecules immobilized on the array surface at a first defined site defined sites, wherein the second cleavage product of the first probe molecule is bound to a second region of the target molecule; and

a cleavage product of a second probe molecule immobilized on the array surface at a second defined site, wherein the cleavage product of the second probe molecule is not bound to a target molecule

wherein the probe molecules have at least one label and at least one selectively cleavable bond between the site of their immobilization on the array surface and the label.

- 2. (Currently amended) The probe array of claim 1, wherein the <u>first and second</u> probe molecules are selected from the group consisting of oligonucleotides, peptides, proteins and their analogues.
- 3. (Currently amended) The probe array of claim 1, wherein the <u>first and second</u> probe molecules are oligonucleotides.
 - 4. (Original) The probe array of claim 3, wherein the oligonucleotides have a length of

Serial No.: 10/789,081 Filed: February 27, 2004

Page: Page 3 of 21

from 10 to 100 bases.

5. (Currently amended) The probe array of claim 1, wherein the first cleavage product of the first probe molecule and the second cleavage product of the first probe molecule are approximately equal in size the selectively cleavable bond is located approximately in the centre between the site of the immobilization of the probe molecule on the array surface and the label.

- 6. (Currently amended) The probe array of claim 1, wherein the <u>cleavage products of the</u> <u>first and second probe molecules are products of non-enzymatic cleavage selectively cleavable</u> <u>bond cannot be selectively cleaved by enzymatic methods</u>.
- 7. (Currently amended) The probe array of claim 1, wherein the <u>cleavage products of he</u> <u>first and second probe molecules are products of cleavage selectively cleavable bond can be selectively cleaved</u> by chemical and/or physical methods.
- 8. (Currently amended) The probe array of claim 1, wherein the <u>cleavage products of the</u> <u>first and second probe molecules are products of cleavage by selectively cleavable bond can be selectively cleaved by the addition of acid anions, base cations, fluoride and/or heavy metal ions.</u>
- 9. (Original) The probe array of claim 8, wherein the heavy metal ions comprise mercury ions and/or silver ions.
- 10. (Currently amended) The probe array of claim 1, wherein <u>cleavage products of the first and second probe molecules are products of cleavage the selectively cleavable bond can be selectively cleaved</u> by photolysis.
- 11. (Currently amended) The probe array of claim 1, wherein the <u>cleavage products of</u> the first and second probe molecules are products of cleavage of probe molecules comprise a

1

Attorney's Docket No.: 15111.0080 / CLON0010 Applicant: Ellinger et al.

Serial No.: 10/789,081 Filed : February 27, 2004

: Page 4 of 21 Page

nucleic acid of the formula A₁-S-A₂, wherein S is a nucleic acid that comprises the at least one selectively cleavable bond, and A₁ and A₂ are any nucleic acids or nucleic acid analogues.

12. (Original) The probe array of claim 11, wherein S is a nucleotide dimer that is bridged by the selectively cleavable bond.

13. (Currently amended) The probe array of claim 12, wherein S is selected from the group consisting of the following dimers having the formulae I and II:

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O; and B represents a nucleobase which is adenine, guanine, cytosine or thymine,

I

Serial No. : 10/789,081 Filed : February 27, 2004 Page : Page 5 of 21

X OPG

O=P-OO

Y OPG,

II

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O, if PG is not a labile protective group; B represents a nucleobase which is adenine, guanine, cytosine or uracil; and PG is selected from the group consisting of H and labile protective groups such as

- 14. (Currently amended) The probe array of claim 1, wherein the <u>cleavage products of</u> the first and second probe molecules are products of cleavage of selectively cleavable bond is a phosphothioate bond.
- 15. (Original) The probe array of claim 1, wherein the label is a detectable unit, which is selected from the group consisting of fluorescent labels, luminescent labels, metal labels, enzyme labels, radioactive labels, polymeric labels and nucleic acids, which are detectable by hybridisation with a labelled reporter probe.
 - 16. (Original) The probe array of claim 15, wherein the detectable unit is coupled to the

Serial No.: 10/789,081

Filed: February 27, 2004

Page : Page 6 of 21

probe molecules via an anchor group.

17. (Currently amended) The probe array of claim 1, wherein the probe molecules are first probe molecules, and wherein said array further comprises second third probe molecules arranged on at least one array element of the probe array, wherein the second third probe molecules have at least one label and no selectively cleavable bond.

- 18. (Currently amended) The probe array of claim 17, wherein the second third probe molecules are oligonucleotides having a defined or randomised sequence.
- 19. (Original) The probe array of claim 1, further comprising an array element having arranged thereon detectable units that are not linked to a probe molecule.
- 20. (Currently amended) The probe array of claim 17, wherein the second third probe molecules are arranged on different array elements which differ in their labelling degree.
- 21. (Original) The probe array of claim 19, wherein the detectable units are arranged on different array elements which differ in their labelling degree.
- 22. (Currently amended) The probe array of claim 1, further comprising third fourth probe molecules which have no affinity or at least no specific affinity to target molecules, wherein the fourth probe molecules are arranged on at least one array element.
- 23. (Currently amended) The probe array of claim 22, wherein the third fourth probe molecules are oligonucleotides with a defined or randomised sequence.
- 24. (Currently amended) The probe array of claim 1, further comprising fourth <u>fifth</u> probe molecules arranged on at least one array element, and which have a specific affinity to

Serial No. : 10/789,081 Filed : February 27, 2004 Page : Page 7 of 21

spiking target molecules which are externally added to the sample.

25. (Currently amended) The probe array of claim 24, comprising array elements distributed over the entire surface of the array, on which said fourth fifth probe molecules are arranged, which have a label and a selectively cleavable bond located between the label and the immobilization site of the probe on the surface and which have a specific affinity to spiking target molecule added externally to the sample or to a target molecule present in the sample in sufficient concentration to lead to a clearly detectable signal.

26.-51. (Canceled)

- 52. (Original) A kit for qualitative and/or quantitative detection of target molecules from a sample by molecular interactions between probe molecules and target molecules on probe arrays, comprising: a) the probe array of claim 1; b) reagents for the selective cleavage of the selectively cleavable bond in the probe molecules; c) hybridisation buffer; and d) optionally, washing buffer.
- 53. (Original) The kit of claim 52, wherein the reagents are selected from the group consisting of heavy metal ions and enzymes.
- 54. (Original) The kit of claim 53, wherein the heavy metal ions are selected from mercury ions and/or silver ions.
 - 55. (Original) The kit of claim 52, further comprising a reaction chamber.
 - 56. (Original) The kit of claim 52, further comprising a detection device.
 - 57. (Original) The kit of claim 52, further comprising a temperature control unit.

Serial No.: 10/789,081 Filed: February 27. 2

Filed: February 27, 2004
Page: Page 8 of 21

58. (Original) The kit of claim 52, wherein the probe array is in the form of a highly integrated autonomous unit.

59.-61. (Canceled)

62. (New) A probe array, comprising: an array surface,

a first probe molecule immobilized on the array surface having at least one label and at least one selectively cleavable bond between the site of immobilization on the array surface and the label, wherein the first probe molecule is bound to a corresponding target molecule; and

a second probe molecule immobilized on the array surface having at least one label and at least one selectively cleavable bond between the site of immobilization on the array surface and the label, wherein the second probe molecule is not bound to a corresponding target molecule; wherein the first and second probe molecules are in contact with a cleaving solution.

- 63. (New) The probe array of claim 62, wherein the first and second probe molecules are selected from the group consisting of oligonucleotides, peptides, proteins and their analogues.
- 64. (New) The probe array of claim 62, wherein the first and second probe molecules are oligonucleotides.
- 65. (New) The probe array of claim 64, wherein the oligonucleotides have a length of from 10 to 100 bases.
- 66. (New) The probe array of claim 62, wherein the selectively cleavable bond of the first probe molecule is located approximately in the centre between the site of the immobilization

Serial No.: 10/789,081

Filed: February 27, 2004

Page: Page 9 of 21

of the probe molecule on the array surface and the label.

67. (New) The probe array of claim 62, wherein the selectively cleavable bond of the first probe molecule cannot be selectively cleaved by enzymatic methods.

68. (New) The probe array of claim 62, wherein the selectively cleavable bond of the first probe molecule can be selectively cleaved by chemical and/or physical methods.

69. (New) The probe array of claim 62, wherein the selectively cleavable bond of the first probe molecule can be selectively cleaved by the addition of acid anions, base cations, fluoride and/or heavy metal ions.

70. (New) The probe array of claim 69, wherein the heavy metal ions comprise mercury ions and/or silver ions.

- 71. (New) The probe array of claim 62, wherein the selectively cleavable bond of the first probe molecule can be selectively cleaved by photolysis.
- 72. (New) The probe array of claim 62, wherein the first probe molecule comprises a nucleic acid of the formula A_1 -S- A_2 , wherein S is a nucleic acid that comprises the at least one selectively cleavable bond, and A_1 and A_2 are any nucleic acids or nucleic acid analogues.
- 73. (New) The probe array of claim 72, wherein S is a nucleotide dimer that is bridged by the selectively cleavable bond.
- 74. (New) The probe array of claim 73, wherein S is selected from the group consisting of the following dimers having the formulae I and II:

Attorney's Docket No.: 15111.0080 / CLON0010

Applicant: Ellinger et al. Serial No.: 10/789,081 : February 27, 2004

Filed Page : Page 10 of 21

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O; and B represents a nucleobase which is adenine, guanine, cytosine or thymine,

wherein X and Y are independently selected from the group consisting of O, NH and S, provided that X and Y are not simultaneously O, if PG is not a labile protective group; B represents a nucleobase which is adenine, guanine, cytosine or uracil; and PG is selected from the group consisting of H and labile protective groups.

75. (New) The probe array of claim 62, wherein the selectively cleavable bond of the

Serial No.: 10/789,081

Filed: February 27, 2004

Page : Page 11 of 21

first probe molecule is a phosphothioate bond.

76. (New) The probe array of claim 62, wherein the label is a detectable unit, which is

selected from the group consisting of fluorescent labels, luminescent labels, metal labels, enzyme

labels, radioactive labels, polymeric labels and nucleic acids, which are detectable by

hybridisation with a labelled reporter probe.

77. (New) The probe array of claim 76, wherein the detectable unit is coupled to the

probe molecules via an anchor group.

78. (New) The probe array of claim 62, wherein said array further comprises third probe

molecules arranged on at least one array element of the probe array, wherein the third probe

molecules have at least one label and no selectively cleavable bond.

79. (New) The probe array of claim 78, wherein the third probe molecules are

oligonucleotides having a defined or randomised sequence.

80. (New) The probe array of claim 62, further comprising an array element having

arranged thereon detectable units that are not linked to a probe molecule.

81. (New) The probe array of claim 78, wherein the third probe molecules are arranged

on different array elements which differ in their labelling degree.

82. (New) The probe array of claim 80, wherein the detectable units are arranged on

different array elements which differ in their labelling degree.

83. (New) The probe array of claim 62, further comprising fourth probe molecules

which have no affinity or at least no specific affinity to target molecules, wherein the fourth

11

Serial No.: 10/789,081 Filed : February 27, 2004

Page : Page 12 of 21

probe molecules are arranged on at least one array element.

84. (New) The probe array of claim 83, wherein the fourth probe molecules are oligonucleotides with a defined or randomised sequence.

85. (New) The probe array of claim 62, further comprising fifth probe molecules arranged on at least one array element, and which have a specific affinity to spiking target molecules which are externally added to the sample.

86. (New) The probe array of claim 85, comprising array elements distributed over the entire surface of the array, on which said fifth probe molecules are arranged, which have a label and a selectively cleavable bond located between the label and the immobilization site of the probe on the surface and which have a specific affinity to spiking target molecule added externally to the sample or to a target molecule present in the sample in sufficient concentration to lead to a clearly detectable signal.

87. (New) A probe array for detection of target molecules in a sample by molecular interactions between probe molecules and target molecules on the probe array, comprising an array surface, and

probe molecules immobilized on the array surface at each of multiple different defined sites, probe molecules of different defined sites being different from one another,

wherein probe molecules of at least one of the defined sites have at least one label, have at least one selectively cleavable bond between the site of their immobilization on the array surface and the label, and do not have a 3' OH group that is extendable by polymerase chain reaction.

88. (New) The probe array of claim 87, wherein the at least one probe molecule is immobilized on the array surface at its 3' end.

Serial No.: 10/789,081 Filed : February 27, 2004

Page: Page 13 of 21

89. (New) The probe array of claim 87, wherein probe molecules of each of multiple defined sites have at least one label, have at least one selectively cleavable bond between the site of their immobilization on the array surface and the label, and do not have a free 3' OH group that is extendable by polymerase chain reaction.